# Epidemiology of organomercury poisoning in Iraq. III. Clinical features and their changes with time

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Three categories of mercury poisoning were defined in the survey described by Al-Mufti et al. (see page 23) and the age-specific incidence rates for these are given. Persons with physical signs consistent with a diagnosis of organomercury poisoning were allocated to categories of severe disability or mild/moderate disability. However, the largest category consisted of persons who had symptoms but no readily elicitable physical signs at the time of the survey. These symptoms followed a consistent pattern with paraesthesia involving the lips and/or circumoral region or trunk and difficulty with walking, described as weakness or unsteadiness of the legs, and in some cases repeated falls, forming the most commonly occurring symptom complex. Mean maximum hair mercury levels differentiated this group very clearly from the group with no symptoms of mercury poisoning. Very few people in the area of low exposure complained of such symptoms; where they did occur they were less well related to the time of the outbreak and showed little tendency to improve. Most people reported improvement in their symptoms by the time of the survey, with more improvement in some symptoms than in others. However, it is not known whether those people with symptoms only at the time of the survey had had at an earlier stage mild signs which had cleared. It was thought unlikely that further substantial improvement would occur in those persons with disability at the time of the survey.

## INTRODUCTION

In attempting to estimate the incidence rate for alkylmercury poisoning in a defined population, clearly defined reproducible criteria for diagnosis must first be established. The clinical manifestations of the more severe cases of poisoning have been fully described and are sufficiently distinctive to ensure a high degree of specificity in diagnosis. In contrast, milder cases where greater skill is required to elicit neurological signs may easily be missed in a field survey where facilities are necessarily limited. However, it might also be possible to define a category of mild poisoning where functional disorder in the form of symptoms exists without abnormal physical signs.

The epidemiological survey of organomercury poisoning in Iraq following the 1972 outbreak described by Al-Mufti et al. (see page 23) was designed to ascertain, inter alia, whether any improvement in symptoms and signs had been or was occurring. The survey was not completed until more than 1 year after the apparent ending of the outbreak, and the

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possibilities were that cases that were mild at that time had been more severe initially and had subsequently improved, or that they had been mild from the very beginning. Little evidence of improvement was found at Minamata[1] but the case described by Hunter et al.[2] showed considerable improvement with time. Similarly, in the Iraq epidemic of 1972 marked improvement in individual severely poisoned subjects has been described.[3]

## METHOD

The clinical criteria by which persons seen on the survey were classified as suffering from alkylmercury poisoning with severe disability or with mild or moderate disability are shown in Table 1. In infants and children below the age of 5 it was not possible to obtain as accurate information on symptoms or to elicit many of the signs. A statement by a parent or close relative that the child was abnormal with apathy or excessive emotional lability, inability to see or loss of ability to walk, with brief clinical verification in the absence of features suggestive of alternative diagnoses and related to the time of the outbreak, was taken as evidence of alkylmercury poisoning.

TABLE 1. DIAGNOSTIC CRITERIA FOR PERSONS SEEN IN THE SURVEY WITH OBJECTIVE EVIDENCE OF ORGANOMERCURY POISONING

| Mercury poisoning with: | |
|---|---|
| Severe disability | Moderate/mild disability |
| Tunnel vision | Moderate constriction of visual fields |
| Blindness | Ataxia - able to walk without assistance |
| Ataxia - unable to walk | Ataxia on finger-to-nose-test |
| Ataxia - able to walk with assistance | Impaired stereognosis |
| Astereognosis | Speech disturbance |
| Speech disturbance with ataxia | Obvious deafness |
| Deafness with ataxia | Emotional instability or apathy |
| Emotional instability or apathy with ataxia | |

In people who had eaten contaminated bread, the presence of paraesthesiae or of a history of some difficulty in walking, without abnormal neurological signs, which had developed in the period of the outbreak was taken as subjective evidence of mercury poisoning. In infants and small children below the age of 5 years a statement by the mother that the child had these symptoms was considered as positive evidence, but these children are not included in the calculation of age-specific incidence rates for the subjective group, owing to the incomplete nature of the data.

Those people who admitted to symptoms were asked whether, at the time of the interview, the complaint had remained unchanged, had become better or had deteriorated since its onset. They were also asked whether the symptoms had started before the end of Ramadan (19 November), between Ramadan and the Prophet's birthday (26 April) - the approximate period of the outbreak - or after that date.

Seventy-five persons who had eaten contaminated bread were re-examined by the survey team about 6 months after the initial visit. A diagnosis was made on the above criteria without knowledge of the diagnosis reached the first time, and the two assessments were then compared.

## RESULTS

In the area of high exposure 30 people were seen with severe disability and 38 with mild or moderate disability. The age distribution of these 68 persons is shown in Table 2, together with the age-specific incidence rate calculated for the population of Hillali. The incidence was highest in older children and young adults and appeared to be very low in children under 5. However, the figure for children under 5 is likely to be a considerable underestimate, owing to the difficulty of making a diagnosis in this age-group in the field survey. Twenty-five of the 30 persons with severe disability had been hospitalized, but 22 of the 38 persons with mild or moderate disability had not been to hospital and were therefore previously unknown cases of alkylmercury poisoning.

TABLE 2. AGE DISTRIBUTION OF CASES OF ORGANOMERCURY POISONING WITH SOME DISABILITY [a]

| Age (years) | No. of cases | Percentage of total No. (i.e., 68) | Rate per 1 000 |
|---|---|---|---|
| <5 | 4 | 6 | 23 |
| 5 - 9 | 16 | 23 | 105 |
| 10 - 14 | 13 | 19 | 123 |
| 15 - 19 | 9 | 13 | 129 |
| 20 - 29 | 6 | 9 | 61 |
| 30 - 49 | 8 | 12 | 52 |
| 50+ | 12 | 18 | 100 |
| Total | 68 | 100 | 75 |

[a] The age-specific rates have been calculated for the surveyed population of the area of high exposure.

There were in addition 9 cases in which it was not found possible to arrive at a diagnosis. The fact that 4 of these were infants aged 6 months or less, and 2 were children aged 3 years, illustrates the problems encountered in making a diagnosis in the very young.

There were 11 women in the severe disability category, all of whom provided hair samples for mercury analysis. The mean maximum hair mercury level for these 11 women was 400 μg/g. Nineteen of the 23 women with mild or moderate disability provided hair samples, and the mean maximum hair level was 209 μg/g.

The frequency of occurrence of certain symptoms recorded in the survey was related to the presence of physical signs elicited in all persons over the age of 5 years. The results are shown in Table 3, where the presence of a sign is shown as a percentage of the frequency of occurrence of the relevant symptom. While deafness was confirmed in only 12 (29% of the 42 persons who complained of this symptom, and ataxia was demonstrated in 44 (30%) of those complaining of weakness or unsteadiness of the legs, blindness was confirmed in 15 (75%) out of 20 persons who claimed they had been unable to see. The absence of a sign does not invalidate the respective symptom however, for signs were sometimes difficult to elicit, particularly acuity of vision in a child. Also, a change in the person's state may have occurred between the time when the symptom developed and the time of the examination.

TABLE 3. A COMPARISON BETWEEN THE PRESENCE OF SYMPTOMS AND SIGNS ELICITED IN ALL PERSONS OVER THE AGE OF 5 YEARS

| Symptom | No. with symptom | No. with sign | % of sign to symptom |
|---|---|---|---|
| Legs weak/unsteady | 146 | 44 | 30 |
| Repeated falls | 91 | 37 | 41 |
| Unable to walk | 73 | 35 | 48 |
| Difficulty in feeding and ataxia | 45 | 18 | 40 |
| Difficulty in feeding and astereognosis | 45 | 20 | 44 |
| Difficulty in dressing and ataxia | 42 | 19 | 45 |
| Difficulty in dressing and astereognosis | 42 | 21 | 50 |
| Change in speech | 75 | 29 | 39 |
| Change in sight | 117 | 40 | 34 |
| Unable to see | 20 | 15 | 75 |
| Change in hearing | 42 | 12 | 29 |

The assessment of those persons who had symptoms of organomercury poisoning, but no abnormal signs at the time of examination, was more difficult. While the individual symptoms elicited in the survey cannot be considered to be specific to organomercury poisoning, their onset in relation to the time of eating contaminated bread was considered relevant. It was unlikely, although not impossible, that sufficient mercury could have been accumulated in the time available to have given rise to symptoms before the end of Ramadan. Similarly, it was again unlikely that sufficient contaminated bread was eaten after the Prophet's birthday to give rise to symptoms of poisoning. Only 20 persons described one or more symptoms which could have been due to poisoning but which occurred before the end of Ramadan. Out of 106 people with persistent headaches, 16 (15%) developed this symptom before Ramadan, although they had eaten contaminated bread only after that date. By contrast, one person out of 90 who complained of repeated falls claimed to have had this symptom from before Ramadan although he too had eaten contaminated bread only after that date. Eight out of 179 persons (4.5%) had paraesthesia involving the extremities before Ramadan and these too claimed to have eaten contaminated bread only afterwards. No person seen in the survey admitted to having eaten contaminated bread after the Prophet's birthday. It was decided that only symptoms originating between the end of Ramadan and the Prophet's birthday would be taken account of in reaching a diagnosis of subjective evidence of mercury poisoning.

The criteria, therefore, for the diagnosis of alkylmercury poisoning on subjective evidence only were symptoms compatible with the diagnosis, including either paraesthesia or difficulty in walking, without the presence of abnormal signs, and first developing between the end of Ramadan and the Prophet's birthday in people who had eaten contaminated bread. There were 123 persons who fulfilled these criteria, and their age and sex distribution is given in Table 4. There were in addition 5 children below the age of 5 years who had

unequivocal symptoms of mercury poisoning, but who have been excluded from the present analysis for the reasons already given.

TABLE 4. AGE DISTRIBUTION OF THOSE CASES WITH SUBJECTIVE EVIDENCE OF MERCURY POISONING ONLY (AGE 5 YEARS AND OVER)

| Age (years) | No. of cases | | | Percentage of total No. (i.e., 123) | Rate per 1 000 |
|---|---|---|---|---|---|
| | Male | Female | Total | | |
| 5 - 9 | 11 | 9 | 20 | 16 | 131 |
| 10 - 14 | 1 | 17 | 18 | 15 | 173 |
| 15 - 19 | 2 | 12 | 14 | 11 | 200 |
| 20 - 29 | 4 | 9 | 13 | 11 | 131 |
| 30 - 49 | 13 | 20 | 33 | 27 | 214 |
| 50+ | 14 | 11 | 25 | 20 | 208 |
| Total | 45 | 78 | 123 | 100 | 133 |

The age-specific rates have been calculated for the surveyed population of Hillali

Of the 123 persons, 108 (88%) complained of paraesthesia, described as a numbness or tingling sensation, and this was the most common symptom. The sensation was complained of most frequently in the hands and feet, with only one person not complaining of involvement of the extremities. Seventy-nine persons (64%) complained of paraesthesia elsewhere over the body, and 62 (50%) of paraesthesia in the circumoral region. In 11 persons with paraesthesia this was the only symptom.

Fifteen people did not have paraesthesia but complained of some difficulty in walking. All but one had experienced weakness or unsteadiness of the legs and all but two had experienced repeated falls, including the person who had not complained of weakness of the legs. In addition to complaining of falls, 11 of the 15 said that they had been unable to walk for some time.

The questions on symptoms involving the legs were designed to assess the presence of ataxia and to grade this by increasing severity, from a feeling of weakness and unsteadiness in the legs, through repeated falls to inability to walk. Weakness of the legs was the second most common complaint, with 73 (59%) of the 123 complaining of this symptom; 40 (32%) complained of repeated falls, and 30 (24%) of having been unable to walk. Only 4 persons complained of repeated falls without, in addition, weakness or unsteadiness of the legs. Altogether 78 (63%) complained of symptoms related to their ability to walk.

The questions related to symptoms involving the arms were similarly designed to assess the presence of ataxia. Since in eating and drinking the use of the hands requires a finer degree of coordination than in dressing, difficulty with these movements appears earlier than difficulty in dressing. There were 20 people (16%) who had experienced difficulty in using their hands while eating or drinking. All had in addition experienced difficulty with their legs. The symptoms were, therefore, reported in the order in which they would have been expected to occur, for in organomercury poisoning the arms are usually involved at a later stage than the legs. This helped to give credence to the veracity of the reported symptoms. Of these 20 people with difficulty in eating and drinking, only 5 found difficulty in

dressing and none complained only of this. Two of these 5 people also complained of difficulty in doing up buttons, but it was realized after the questionnaire had been designed that this was a poor response to elicit, as few of the rural population have buttons on their clothes.

Six people (5%) complained that they had noticed a change in their ability to speak clearly. All had in addition paraesthesia and 5 of them had symptoms relating to ataxia. All but one of the 33 persons (27%) who had complained of a change in vision also had paraesthesia and 25 of these had symptoms related to ataxia. Of the 9 people (7%) who complained of a change in ability to hear, 8 had symptoms related to ataxia and 6 had both paraesthesia and ataxia. Twenty-eight people (23%) complained of a rash during the relevant period and, of these, 20 had both paraesthesia and symptoms related to ataxia. There were 69 people (56%) with persistent pain in the limbs; 65 of these had paraesthesia and 47 had symptoms related to ataxia. Sixty people (49%) had persistent headaches; of these, 57 had paraesthesia and 38 had symptoms related to ataxia.

The mean maximum hair mercury level in 33 males (all with short hair) in this group was 22 $\mu g/g$ and in 67 females 321 $\mu g/g$. In the remaining 23 subjects hair mercury was not estimated. All but 4 of the estimations in males were performed only on the first inch of hair, this being the only material available, whilst in the females these maximum values were found in the fourth to sixth-inch segments of hair. Forty-six females (69%) with subjective evidence of poisoning had hair mercury levels above 100 $\mu g/g$ and 9 of these had hair mercury levels above 500 $\mu g/g$. Only 3 females in the subjective poisoning category had maximum hair mercury levels below 10 $\mu g/g$.

The majority considered that their symptoms had improved since the onset. The total number of positive replies in the area of high exposure to each of the 15 questions on symptoms is listed in Table 5, together with the proportion who claimed that they were better at the time of the survey. Some interesting differences in these symptoms can be seen. Of those who were unable to walk, 66 (93%) said that they had improved, but only 12 (60%) out of 20 of those who said they had been unable to see thought that they had improved. Of those persons complaining of paraesthesia of the extremities 162 (86%) also claimed to have improved. Only a small number of people in the area of low exposure complained of paraesthesia but, by contrast, none of them thought they had improved. There were 11 persons with numbness of the extremities in this category.

The clinical diagnostic category was compared in 77 persons who had eaten contaminated bread and who were seen on a second occasion approximately 6 months after the first (Table 6). The assessment on the second occasion was made without knowledge of that made on the first. In 52 cases (67%) the category remained unchanged. There was improvement in category in 17 cases (22%) and deterioration in 6 cases (8%). In 2 cases it was not possible to determine the diagnosis on the second occasion. Thirteen of the 17 cases showing improvement had only subjective evidence of poisoning the first time they were seen.

## DISCUSSION

It seems likely that the clinical picture of organomercury poisoning in the Iraq epidemic changed with time, improvement having been shown in many of the cases studied. A difference from the Minamata cases in this respect may have been due to the different pattern of accumulation of mercury in the two outbreaks. In Iraq, heavy exposure occurred for a relatively short time, and the pattern of mercury accumulation may have resembled in some ways that in industrially exposed cases, who have shown gradual improvement after cessation of exposure. There are obvious difficulties in assessing the course of an outbreak in a study performed approximately 1 year after the end of exposure.

TABLE 5. TOTAL ENUMERATION OF SYMPTOMS COMPLAINED OF IN HILLALI, IN ALL PERSONS WITH MERCURY POISONING, WITH PERCENTAGE WHO CONSIDERED THEY HAD IMPROVED BY THE TIME OF THE SURVEY

| Symptom | No. with symptoms | % improvement |
|---|---|---|
| Paraesthesia: | | |
| circumoral | 118 | 90 |
| extremities | 189 | 86 |
| elsewhere | 141 | 89 |
| Persistent limb pains | 133 | 80 |
| Persistent headaches | 110 | 79 |
| Weakness or unsteadiness of legs | 143 | 94 |
| Repeated falls | 91 | 94 |
| Inability to walk | 71 | 93 |
| Difficulty in feeding | 44 | 87 |
| Difficulty in dressing | 41 | 88 |
| Change in speech | 74 | 95 |
| Change in sight | 113 | 79 |
| Inability to see | 20 | 60 |
| Change in hearing | 40 | 77 |
| History of rash | 64 | 95 |

TABLE 6. CLINICAL DIAGNOSIS ON SECOND VISIT COMPARED WITH THAT MADE ON FIRST VISIT, 6 MONTHS EARLIER

| 2nd visit compared with 1st visit | No. in each category | | | | | Total |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | |
| No change | 33 | 4 | 5 | 10 | 0 | 52 |
| Improvement | 13 (2) | 2 (3) | 2 (4) | | | 17 |
| Deterioration | | 4 (1) | 1 (1) | 1 (1) | | 6 |
| Unable to determine | | | | | 2 (1,2) | 2 |

Figures in parentheses indicate category on first visit.

The more severe cases of poisoning, those with gross neurological defect, are unlikely to have shown much recovery and it is probable that these cases were correctly enumerated in the survey. Neither would these cases with disability be expected to show substantial improvement in the future. Cases with a minor neurological defect following the eating of contaminated bread may have improved sufficiently by the time of the survey to have lost their abnormal signs and so be classified as cases of poisoning with subjective evidence only, obtained from the history. Alternatively, a minor neurological deficit may have been missed in the survey because of the difficulty of eliciting neurological signs under field conditions. It appears possible, therefore, that the category "Subjective mercury poisoning" was overestimated, at the expense of the category "Mild or moderate mercury poisoning". Another possible reason for an overestimate could be that in some persons the symptoms were due to some other disorder. As might be expected, a number of the symptoms were found also in persons who were not exposed to organomercury. It would be reasonable to reduce the estimate of subjective mercury poisoning to the extent by which the symptoms on which the diagnosis was based were found in this group. However, the symptoms were not common in the area of low exposure, and such a reduction would not materially reduce the estimate of the number of cases.

The question remains whether, following the absorption of alkylmercury compounds, a category of poisoning can be defined in which symptoms such as paraesthesiae, headaches, persistent pain and weakness of the limbs predominate with little or no evidence of neurological damage on clinical examination. It is likely that such is in fact the case. The category observed without neurological signs at the time of the examination had a characteristic pattern of symptoms in which paraesthesiae of the extremities, with in some cases involvement of the circumoral region, and persistent pain, weakness and unsteadiness of the legs, persistent headaches and some subjective deterioration in vision predominated. The persons in this group had eaten less contaminated bread than those with neurological disability and their blood and hair mercury levels were intermediate between those found in the low exposure group and in the group with disability.

The survey showed that in the area of high exposure a number of people had some disability and a large number of others, additional to those who had been diagnosed in hospital, had symptoms compatible with organomercury poisoning.

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RESUME

EPIDEMIOLOGIE DES INTOXICATIONS PAR ORGANOMERCURIELS EN IRAK

III. CARACTERISTIQUES CLINIQUES ET LEURS MODIFICATIONS AVEC LE TEMPS

Le document indique les taux d'incidence par âge des trois catégories d'intoxications par composés mercuriels définies dans l'enquête décrite par Al-Mufti et al. (voir p. 23). Les sujets présentant des signes physiques correspondant à un diagnostic d'intoxication par organomercuriels ont été répartis en deux catégories: incapacité grave et incapacité

légère/modérée. La catégorie la plus nombreuse était composée de sujets ressentant des symptômes au moment de l'enquête mais ne présentant pas de signes physiques faciles à déceler. Les symptômes étaient assez constants - l'ensemble le plus courant comprenant de la paresthésie des lèvres et/ou de la région périorale ou du tronc, des difficultés de la marche dues à une faiblesse ou à une instabilité des jambes et, dans certains cas, des chutes répétées. Les concentrations moyennes maximales de mercure dans les cheveux permettaient de différencier nettement ce groupe de celui des sujets n'éprouvant pas de symptômes d'intoxication. Dans la zone de faible exposition, très peu de sujets se sont plaints de tels symptômes; ces symptômes n'étaient pas nettement en rapport avec la date de l'épisode d'intoxication et la tendance à l'amélioration était faible. Au moment de l'enquête, la plupart des sujets ont signalé une amélioration de leurs symptômes, cette amélioration intéressant toutefois certains symptômes plus que d'autres. On ne sait pas cependant si les personnes qui au moment de l'enquête n'éprouvaient que des symptômes subjectifs n'avaient pas présenté précédemment des signes légers qui auraient disparu par la suite. Il a semblé peu probable que les sujets souffrant d'incapacité au moment de l'enquête puissent connaître ultérieurement une amélioration importante de leur état.

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